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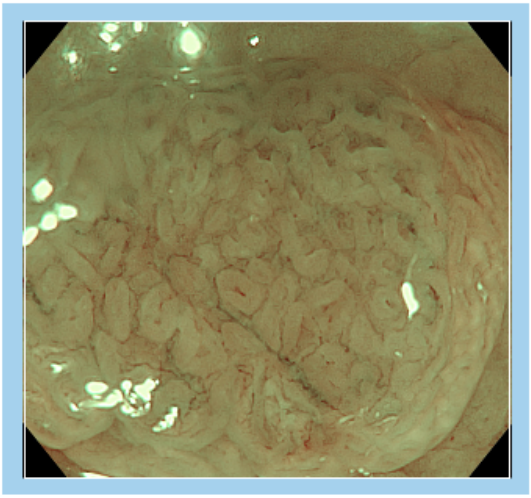
LA CROMOENDOSCOPIA VIRTUAL EN LA DETECCIÓN DE DISPLASIAS DE COLON EN PACIENTES CON ENFERMEDAD INFLAMATORIA INTESTINAL. REVISIÓN SISTEMÁTICA

Estudios que comparan directamente la cromoendoscopia con colorantes (CEC) con la cromoendoscopia virtual (CVC) para detectar displasias en EII de colon:

- 12 estudios seleccionados de 141 resultados.
- Detección similar de displasias con ambas técnicas.
- Menores tiempos de exploración con CEV.

La CEV se perfila como alternativa válida para el cribado de displasias en nuestros pacientes.



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Virtual chromoendoscopy for the identification of colonic dysplasia in patients with inflammatory bowel disease. A systematic review

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Texto visual abstract traducido

VIRTUAL CHROMOENDOSCOPY IN THE IDENTIFICATION OF COLONIC DYSPLASIA IN patientS WITH INFLAMMATORY BOWEL DISEASE. A SYSTEMATIC REVIEW

Studies directly comparing dye-spraying chromoendoscopy (DCE) *versus* virtual chromoendoscopy (VCE) for the detection of colonic dysplasia in IBD:

- 12 studies selected out of 141 results.
- Similar dysplasia identification rates with both techniques.
- Lower examination times with VCE.

VCE is taking shape as a valid alternative for dysplasia screening in our patients.

ABSTRACT

Introduction: patients with inflammatory bowel disease (IBD) in the colon have a higher risk for colorectal cancer (CRC). Virtual chromoendoscopy (VCE) allows identification and assessment of colonic dysplasia, which might displace dye-based chromoendoscopy (DCE) as the endoscopist's technique of choice for these patients within endoscopic surveillance programs.

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Objective: to analyze the best evidence available on the usefulness of VCE *versus* DCE for dysplasia identification in patients with long-standing colonic IBD.

Material and methods: a qualitative, PRISMA 2020-based systematic review of the literature was carried out in the PubMed, Science Direct, and Scielo databases until June 2023. Clinical trials, case-control studies, comparative studies, and crossover studies in English or Spanish were included that directly compared DCE *versus* VCE for the screening of colonic dysplasia in patients with IBD. The Quality Assessment of Diagnostic Accuracy studies (QUADAS) 2 was used for assessing study quality. The selected studies were evaluated by 2 independent researchers, who entered their abstracted results into a database.

Results: out of 141 identified studies 9 were selected that compared DCE with VCE (1131 patients included). Six studies are prospective, randomized, controlled trials; 2 are retrospective case-control studies; and 1 is a prospective comparative study. VCE showed a dysplasia detection ability similar to that of DCE, albeit with shorter examination times (8 studies; 985 patients). Factors associated with dysplasia identification included lesions in the right colon (3 studies; 581 patients); non-polypoid lesions (1 study; 210 patients) and/or lesions with Kudo's type III-V pit patterns (2 studies; 254 patients); and patient age (1 study; 129 patients).

Conclusions: VCE may be an alternative to DCE for CRC screening in patients with long-standing IBD, with similar detection ability for colonic dysplasia and the benefit of shorter procedure times. Currently available evidence is limited in this regard given the small numbers of patients in the relevant studies, hence further research is necessary with greater numbers of included subjects.

Keywords: Colonoscopy. Colitis-associated neoplasm. Inflammatory bowel diseases. Chromoendoscopy.

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INTRODUCTION

The risk for colorectal cancer (CRC) among patients with colonic inflammatory bowel disease (IBD) is 1.5-2 times higher than in the general population (1). While this risk is higher the longer the condition has been present (2-4), its incidence has decreased to 1 %, 2 % and 5 % for 10 years, 20 years and over 20 years of disease duration, respectively, over the past few decades. This decrease has been similar for both ulcerative colitis and Crohn's disease (5). However, in 1.2 % of patients with CRC the malignancy is currently associated with IBD. Furthermore, when compared to the general population, these patients are on average 15 years younger at diagnosis, and survival at 5 years is up to 14 points lower in those younger than 65 years of age (6).

CRC prevention in IBD is based on adequate control of inflammatory activity and endoscopic surveillance (7). The latter is associated with a lower incidence of both interval cancer and advanced cancer, and lower CRC-related mortality (8-10). Therefore, different scientific societies have developed highly similar guidelines to indicate when screening should be started in these patients and with which periodicity (11). Despite this, adherence to screening programs is usually low, only one third of patients comply adequately, even less among high-risk patients (12).

While the available evidence was not very high, in 2015 the SCENIC international consensus considered that, *versus* white-light endoscopy with random biopsy sampling, dye-spraying chromoendoscopy (DCE) with targeted biopsy collection is the best technique for the identification of dysplasic lesions (13). Later, some studies have suggested that high-definition endoscopy might be supplementary or even an alternative to DCE (14,15). Furthermore, we have now had virtual chromoendoscopy (VCE) techniques for some years, techniques that allow to improve the visibility of superficial structures without any dyes, and assess blood vessel morphology. We are primarily referring to Narrow Band Imaging (NBI), iSCAN, and Flexible Imaging Color Enhancement (FICE), but others also exist including Autofluorescence Imaging (AFI), Blue Laser Imaging (BLI), and Linked Color Imaging (LCI) (16). Interestingly, there is a significant dearth of knowledge on the usefulness of VCE techniques for dysplasia screening in patients with long-standing colonic IBD. In fact, since no evidence exists

against its use, the latest guide by the European Society of Gastrointestinal Endoscopy (ESGE) includes DCE as potential screening technique for these patients (17). Bearing this in mind, it is appropriate to assess the usefulness of VCE *versus* DCE in CRC screening programs for patients with long-standing IBD in order to optimize the process and get to know which technique may be best for early dysplasia identification.

The primary objective of this review is to analyze the studies that have directly compared DCE *vs* VCE. The aim is to find out the most effective technique in terms of identification of colonic dysplastic lesions. As secondary endpoints examination times and both clinical and endoscopic factors associated with colonic dysplasia identification are also evaluated.

MATERIAL AND METHODS

A qualitative systematic review of the literature till June 2023 was performed following the PRISMA 2020 recommendations (Supplementary Tables 1 and 2) (18). We analyzed the studies (in Spanish and/or English) identified in 3 validated open-access information sources (databases — PubMed, Science Direct, Scielo) that compared the DCE and VCE techniques for the screening of dysplasia in patients with IBD. Supplementary table 3 shows the complete search strategy that was used.

Studies were selected that met the following *inclusion criteria:* 1) clinical trial, case-control study, comparative study or crossover study design; 2) comparing DCE *vs* VCE techniques in dysplasia screening; and 3) including patients with long-standing IBD (Crohn's disease and/or ulcerative colitis). *Exclusion criteria* included: 1) other designs such as meta-analysis, editorials, clinical guidelines, literature reviews, case reports or conference abstracts; 2) studies with only an abstract accessible; 3) studies using endoscopic techniques other than DCE and VCE; 4) studies with duplicate information and/or irrelevant to the review's aim. The literature was selected independently by 2 researchers to prevent bias — title, abstract and full text were reviewed, and any disagreements were resolved by consensus. From each study information was collected regarding authors, year of publication, country of conduction, type of design,

number of included patients, number of dysplasias (including low-grade dysplasia, high-grade dysplasia and carcinoma), number and percentage of patients with dysplasia, examination duration (total and colonoscope withdrawal) and risk factors associated with colonic dysplasia. A database was developed in Excel to synthesize and list study results.

This review includes studies with different designs, randomized or otherwise. The quality of the methodology and the potential biases of the studies selected were independently evaluated by 2 reviewers using the Quality Assessment of Diagnostic Accuracy studies (QUADAS) 2 scale (19). This tool considers four key domains: patient selection, index test, reference standard test, and finally patient flow through the study as well as the timing of both the index and reference tests (flow and times). Each domain is evaluated in terms of bias risk, and concerns about applicability are also addressed for the first three domains.

RESULTS

Studies included

Figure 1 summarizes the article selection process. From a total of 141 initially identified studies 9 papers were eventually collected, which compared DCE with VCE in patients with IBD; the total number of patients included was 1131. Table 1 shows the most relevant study characteristics. Six studies are prospective randomized controlled trials (2 of them are tandem studies) (20-25), 2 are retrospective case-control studies (26,27), and 1 is a prospective comparative tandem study (28). Most studies used indigo carmine staining (20,24-27) whereas most commonly used VCE techniques included iSCAN in 4 studies (20,23,25,27) and NBI in 3 studies (21,25,28), for a total of 363 patients and 169 patients, respectively. Vleugels et al. reported their study results in 2 publications (22,29).

Synthesis of results

Ability to detect colonic dysplasia

Regardless of VCE technique, the 9 studies that were selected showed no significant differences in ability to detect colonic dysplasia between modalities, with dysplasia being identified in over 10 % of patients in all cases (20-28) (Table 2).

Examination time

Endoscopic examination times were analyzed in 8 of the 9 studies selected, with a total of 985 patients (20-26,28) (Table 3). Overall, time savings of 4-11 minutes in endoscope withdrawal and 5-8.5 minutes in total examination time were obtained for VCE. These differences were statistically significant in 7 studies regardless of the technology used (20-26). In the study by Efthymiou et al. (28) examination times were similar, which was attributed to the greater difficulty entailed in the interpretation of NBI images compared to methylene blue staining.

Clinical and endoscopic factors associated with colonic dysplasia

Table 4 lists the risk factors associated with the presence of colonic dysplasia in the 5 studies that analyzed them (20,23,26,28,29), the most common risk factor being lesions identified in the right colon (3 studies; 581 patients) (23,26,29). Other identified factors included presence of lesions with non-polypoid morphology (1 study; 210 patients) (29) and/or lesions with Kudo's type III-V pit patterns (2 studies; 254 patients) (28,29), as well as older age (1 study; 129 patients) (20).

Quality assessment

We found that in the 6 randomized controlled studies that were selected general, vague comments were made about their randomization methods, particularly in the studies by Gulati et al. (24) and Pellisé et al. (25). Despite this, the groups resulting from randomization were well balanced in all the studies, and the researchers were able to meet their goals. These studies could not be truly blinded since colonoscopy was used in all of them, but such lack of subject blinding was deemed unlikely to have

a major impact on the results. The analyzed groups were comparable at study onset and all patients complied with their assigned interventions. The 3 non-randomized studies offer appropriate measures to meet their specified goals (26-28), although the study by Gasia et al. (27) did not consider confounding factors in the analysis of results. The details of bias assessment for each individual study and as a whole are shown in supplementary figures 1 and 2.

DISCUSSION

Both DCE and VCE are endoscopic techniques that may help the endoscopist to identify dysplasias in patients with long-standing IBD. Both have a number of advantages and disadvantages that may have an impact on its usability in daily practice, hence understanding their real usefulness seems appropriate. To this end a systematic review of the literature was undertaken by analyzing studies directly comparing DCE *vs* VCE when used for this purpose. We found that VCE has a diagnostic yield similar to that DCE when it comes to detecting colonic dysplasias in these patients, with VCE representing a technique that requires a shorter examination time.

Traditionally, the technique used for screening dysplasia in individuals with colonic IBD have been based both on mucosal examination with targeted sampling of visible lesions and on random biopsies to identify invisible dysplasia (30). Advances in endoscopic techniques have managed to visualize previously unseen dysplastic lesions. Thus, the SCENIC consensus established in 2015 that DCE with targeted biopsies was the technique of choice for these patients (13), a recommendation also supported in 2021 by the *Grupo Español de Trabajo en Enfermedad de Crohn y Colitis Ulcerosa* (GETECCU) (11). Nevertheless, studies remain that support using random biopsy in selected settings, including patients with a history of malignancy, concurrent primary sclerosing cholangitis, or active inflammation during endoscopy (31,32). Recently, the development of high-definition colonoscopy has even raised debate on the redundancy of DCE given the fact that most dysplasias are visible with this technology (14,15).

The scenario of CRC surveillance in IBD has been further enriched with the development of VCE, a technique with no dyes involved, able to provide instantaneous digital staining by merely pushing a button on the endoscope itself, thus enhancing mucosal and underlying vascularization features. The studies evaluated in this systematic review are consistent in that, generally speaking, DCE and VCE do not differ significantly in terms of endoscopic surveillance yield in patients with IBD, regardless of modality.

We found that 2 of the 4 papers using iSCAN as VCE technique are prospective randomized controlled clinical trials where no differences were spotted in dysplasia identification rates (20,23), neither in the analysis by lesion (number of lesions identified by each technique) nor in the analysis by patient (number of patients identified by each technique with at least 1 dysplastic lesion). The remaining 2 papers refer to retrospective studies, which again did not find any differences between both techniques (26,27).

As regards NBI, Bisschops et al. found no significant differences in terms of number of lesions identified per procedure or the analysis by patient (21). However, the study by Efthymiou et al. showed thet DCE detected more lesions than NBI, and NBI had a dysplasia detection failure rate of 10 %, albeit without statistically significant differences, which may likely result from small sample size (28). With these results, the authors do not recommend using NBI for endoscopic surveillance in patients with IBD. Pellisé et al. (25) also do not recommend using NBI given the possibility of having fewer intraepithelial neoplasms identified, but again differences were not statistically significant. These 3 studies were included in the meta-analysis by Har-Noy et al., published in 2017 (33), which showed that NBI was not, statistically, significantly different from DCE in terms of dysplasia identification, bearing in mind that the number of dysplastic lesions identified in these studies was small, which precluded a more robust result.

In the case of AFI for VCE, the study by Vleugels et al. identified patients with dysplasia similarly (22), albeit AFI detected a greater number of lesions with dysplasia, and also exhibited greater accuracy for real-time dysplasia prediction (29). Finally, FICE

displayed a higher diagnostic accuracy *versus* DCE, and was the technique patients preferred according to the crossover study by Gulati et al (24). In this study patients considered that VCE was a more dignified procedure (no contrast agents, shorter procedural time, less bloating/cramping) and were more willing to undergo this examination than DCE. These aspects may be relevant for ensuring adequate adherence to screening programs, particularly in high-risk patients requiring ever more thorough, frequent surveillance strategies.

Since dyes are no longer needed, it stands to reason that VCE will require shorter examination times. Thus, 8 studies included in the review base their results on examination time measurements (20-26,28). VCE significantly reduced the total procedural and/or withdrawal times necessary to complete the colonoscopic assessment in all but the studies by Efthymiou et al. and Iacucci et al. (23,28), which was supported by the meta-analysis carried out by El-Dallal et al., reported in 2020 (34). This may be due to the longer procedural time associated with dye administration and excess dye suctioning, as well as the potential identification of a greater number of lesions without pathological significance upon examination. Overall, in all 8 studies colonoscope withdrawal time and total examination time decreased by some 7 minutes and 6 minutes on average, respectively. In 2 studies (21,26) withdrawal time kept on being shorter in the VCE group when patients were grouped together according to the total number of lesions resected during the procedure, indicating that the difference in withdrawal time is more related to endoscopic technique than it is to the number of detected lesions.

Adherence is currently low to endoscopic dysplasia screening programs for patients with IBD, especially among higher-risk groups, as was demonstrated in the study by Ballester et al. (12). In this Spanish multicenter study patients complying with adequate endoscopic follow-up were seen to have a higher rate of advanced lesion identifications, and detection occurred earlier in the course of their disease. Therefore, it is necessary to increase patient adherence to dysplasia screening programs and also that endoscopists perform their technique of choice in the most appropriate way. Given the usual saturation in digestive endoscopy units and the increasing availability of advanced technology for use in routine practice, the findings of this review might be

an important push for endoscopists to adopt VEC as a routine technique, relegating DCE to those situations in which VEC is not available. In any case, none of the aforementioned VEC techniques can be recommended over the others.

Another objective of this review was to determine the clinical and endoscopic characteristics associated with the presence of colonic dysplasia (20,23,26,28,29). Lesion location in the right colon was associated with presence of dysplasia in 3 of the studies analyzed (23,26,29). On the other hand, the assessment of Kudo's pit pattern during endoscopy to predict histology in IBD patients remains controversial due to potential distortion of the mucosa by inflammation, with accuracy in this respect being low in the study by Efthymiou et al. (28). As dye spraying may also hinder the reading of this pattern, Iacucci et al. only recommend pit pattern analysis when using high-definition endoscopes with or without VCE (23), even without magnification, but in the absence of staining. Regarding the clinical characteristics of patients, the only independent risk factor detected was age (20).

At this time there is insufficient data to suggest that VCE is superior to DCE. However, there is further evidence pointing to the fact that the lack of differences between the two might favor the former when taking into account the benefit of a shorter procedural time. In fact, in 2019 the ESGE came to definitively support VCE with targeted biopsies as an alternative to DCE for the surveillance of colon neoplasms in IBD patients (17). There are also data on patient satisfaction and procedure costs in the study by Gulati et al. (24). In said study validated questionnaires were administered immediately after endoscopy and at 48 hours, showing a greater preference for VCE, with VCE being also cheaper than DCE, this cost being related to endoscopist working time, consumables used, and subsequent histopathological processing. These reasons should also be taken into account when supporting the use of VCE in these patients.

In recent years, techniques using computer-assisted diagnosis (CADe) systems have begun to be used to detect dysplasia in patients with IBD (35,36), techniques that even allow histological diagnosis in vivo, which may lead to higher-quality endoscopy and a reduction in unnecessary polypectomies. The encouraging results obtained to date will

undoubtedly lead to further research in this field, which could pave the way for a completely new strategy in the field of both diagnostic and therapeutic colonoscopy (37).

During the course of this review some limitations were observed. VCE is a technique of recent development and applicability. Therefore, the number of studies performed in this regard is very small. Likewise, there is heterogeneity amongst the different studies concerning the conditions under which colonoscopy is performed and sample size, which does not allow firm conclusions to be drawn. Nevertheless, all these limitations were taken into account when formulating the conclusions of the review.

In summary, VCE is presented as an alternative to DCE for screening colonoscopies in patients with long-standing IBD, with similar results in colonic dysplasia identification and the advantage of shorter examination times. Further studies are needed to evaluate each of the existing VCE techniques, given the scarcity of adequately designed studies and their low numbers of included patients.

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Revista Española
de Enfermedades Digestivas
The Spanish Journal
of Gastroenterology

Table 1. Characteristics of the 9 studies selected

Authors	Publication year	Country	Design	DCE technique (*n*)	VCE technique (*n*)
López-Serrano A, et al. (26)	2021	Spain	Retrospectivo; casos y controles	IC (98)	iSCAN 1-3 (93)
González-Bernardo O, et al. (20)	2020	Spain	PRCT	IC (67)	iSCAN 1 (62)
Vleugels JLA, et al. (22)	2018	Netherlands and United Kingdom	PRCT	IC/MB (105)	AFI (105)
Gulati S, et al. (24)	2018	United Kingdom	Tandem PRCT	IC (48)	FICE (48)
Iacucci M, et al. (23)	2018	Canada	PRCT	IC/MB (90)	iSCAN 2-3 (90)
Bisschops R, et al. (21)	2017	Belgium and Canada	PRCT	MB (66)	NBI (65)
Gasia MF, et al. (27)	2016	Canada	Retrospective; case-control	IC (28)	iSCAN 1-2-3 (118)
Efthymiou M, et al. (28)	2013	Australia	Prospective, tandem comparison	MB (44)	NBI (44)
Pellisé M, et al (25)	2011	Spain	Tandem PRCT	IC (60)	NBI (60)

DCE, dye-based chromoendoscopy. VCE, virtual chromoendoscopy. *n*, number of patients included. PRCT, prospective randomized controlled trial. IC, indigo carmine. MB, methylene blue. AFI, autofluorescence imaging. FICE, flexible imaging color enhancement. NBI, narrow band imaging.

Table 2. Identified colonic dysplasias in the 9 studies selected

Authors	Patients with dysplasia		Number of dysplasias	
	DCE: *n* (%)	VCE: *n* (%)	DCE	VCE
López-Serrano A, et al. (26)	12 (12.2)	9 (9.7)	32	12
González-Bernardo O, et al. (20)	9 (13.4)	7 (11.3)	12	7
Vleugels JLA, et al. (22)	20 (19.1)	13 (12.4)	38	14
Gulati S, et al. (24)	6 (12.5)	3 (6.25)	9	5
Iacucci M, et al. (23)	22 (22.2)	14 (15.5)	16	11
Bisschops R, et al. (21)	14 (21.2)	14 (21.5)	31	21
Gasia MF, et al. (27)	9 (32.1)	15 (12.7)	9	11
Efthymiou M, et al. (28)	11 (25.0)	10 (22.7)	20	17
Pellisé M, et al (25)	11 (18.3)	12 (20.0)	12	10

DCE, dye-based chromoendoscopy. VCE, virtual chromoendoscopy. *n*, number of patients.

Table 3. Procedure times for the 8 studies analyzed*

Authors	Total time†		Withdrawal time†	
	DCE	VCE	DCE	VCE
López-Serrano A, et al. (26)	19	14	13	9
González-Bernardo O, et al. (20)	20	14	15	10
Vleugels JLA, et al. (22)	38	25	29	18
Gulati S, et al. (24)			20	14
Iacucci M, et al. (23)	19	14	13	9
Bisschops R, et al. (21)	32	27	25	18
Efthymiou M, et al. (28)	13	13		
Pellisé M, et al (25)			27	16

DCE, dye-based chromoendoscopy. VCE, virtual chromoendoscopy. *Significant differences ($p < 0.01$) were found in all studies except those by Efthymiou M, et al. (28) and Iacucci M, et al. (23) †Mean number of minutes.

Table 4. Results according to the dysplasia risk factors identified in 5 studies

Authors	Location in the right colon*	Lesion morphology*		Age
		Non-polypoid	Kudo's type III-V pit patterns	
López-Serrano A, et al. (26)	4.04 (1.11-14.65)			
González-Bernardo O, et al. (20)				1.05 (1.01-1.09)
Vleugels JLA, et al. (29)	2.23 (1.01-4.90)	2.59 (1.15-5.82)	11.54 (5.17-25.76)	
Iacucci M, et al. (23)	4.04 (1.11-14.65)			
Efthymiou M, et al. (28)			Accuracy = 74 %[†]	

*Odds ratio (95 % confidence interval). [†]95 % confidence interval = 0.68–0.80; $p = 0.04$ (Pearson's χ^2 test).

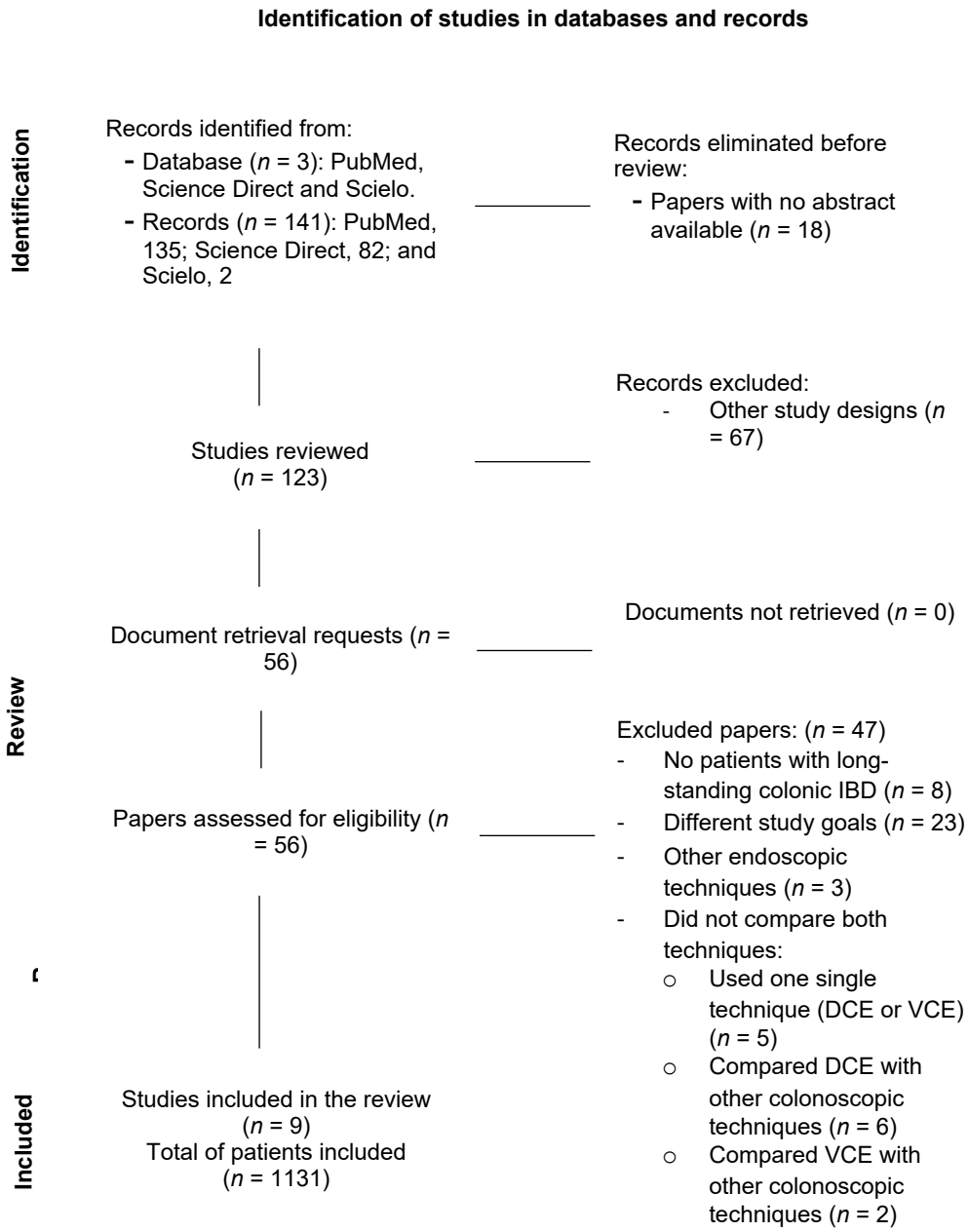


Figure 1. PRISMA 2020 flowchart of the selection process of papers for systematic reviews (18) (IBD, inflammatory bowel disease. DCE, dye-spraying chromoendoscopy. VCE, virtual chromoendoscopy).

Supplementary Table 1. **PRISMA abstract checklist**

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Not applicable
Registration	12	Provide the register name and registration number.	Not

Section and Topic	Item #	Checklist item	Reported (Yes/No)
			applicable

Section and Topic	Item #	Checklist item	Reported (Yes/No)

Section and Topic	Item #	Checklist item	Reported (Yes/No)
			Not applicable

Font: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. DOI: 10.1136/bmj.n71 (18).

Supplementary Table 2. **PRISMA checklist**

Section and Topic	Item #	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	See the corresponding checklist provided
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5 and 6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	5

Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Not applicable
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Not applicable

	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not applicable
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	6
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	6
Study characteristics	17	Cite each included study and present its characteristics.	6
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Not applicable
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	6 and 7

	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not applicable
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	8
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	8
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	6 and 7
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	8
	23b	Discuss any limitations of the evidence included in the review.	10 and 11
	23c	Discuss any limitations of the review processes used.	13
	23d	Discuss implications of the results for practice, policy, and future research.	12
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	The review was not registered
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	A protocol was not prepared
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	1
Competing interests	26	Declare any competing interests of review authors.	1

Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Not applicable

Font: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. DOI: 10.1136/bmj.n71 (18).

Supplementary Table 3. Search criteria for PubMed, Science Direct and Scielo

PubMed:

(("inflammatory bowel diseases"[MeSH Terms] OR ("inflammatory"[All Fields] AND "bowel"[All Fields] AND "diseases"[All Fields]) OR "inflammatory bowel diseases"[All Fields] OR ("inflammatory"[All Fields] AND "bowel"[All Fields] AND "disease"[All Fields]) OR "inflammatory bowel disease"[All Fields] OR ("colitis, ulcerative"[MeSH Terms] OR ("colitis"[All Fields] AND "ulcerative"[All Fields]) OR "ulcerative colitis"[All Fields] OR "colitis ulcerative"[All Fields]) OR ("crohn disease"[MeSH Terms] OR ("crohn"[All Fields] AND "disease"[All Fields]) OR "crohn disease"[All Fields])) AND ("colitis associated neoplasms"[MeSH Terms] OR ("colitis associated"[All Fields] AND "neoplasms"[All Fields]) OR "colitis associated neoplasms"[All Fields] OR ("colitis"[All Fields] AND "associated"[All Fields] AND "neoplasms"[All Fields]) OR "colitis associated neoplasms"[All Fields] OR ("colorectal neoplasms"[MeSH Terms] OR ("colorectal"[All Fields] AND "neoplasms"[All Fields]) OR "colorectal neoplasms"[All Fields])) AND ("colonoscopy"[MeSH Terms] OR "colonoscopy"[All Fields] OR "colonoscopies"[All Fields] OR ("endoscopie"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopies"[All Fields] OR "endoscopy s"[All Fields])) AND ("methylene blue"[MeSH Terms] OR ("methylene"[All Fields] AND "blue"[All Fields]) OR "methylene blue"[All Fields] OR ("indigo carmine"[MeSH Terms] OR ("indigo"[All Fields] AND "carmine"[All Fields]) OR "indigo carmine"[All Fields]) OR ("colouring agents"[All Fields] OR "coloring agents"[Pharmacological Action] OR "coloring agents"[MeSH Terms] OR ("coloring"[All Fields] AND "agents"[All Fields]) OR "coloring agents"[All Fields]) OR ("narrow band imaging"[MeSH Terms] OR ("narrow"[All Fields] AND "band"[All Fields] AND "imaging"[All Fields]) OR "narrow band imaging"[All Fields]) OR ("image enhancement"[MeSH Terms] OR ("image"[All Fields] AND "enhancement"[All Fields]) OR "image enhancement"[All Fields]) OR ("optical imaging"[MeSH Terms] OR ("optical"[All Fields] AND "imaging"[All Fields]) OR "optical imaging"[All Fields] OR

("autofluorescence"[All Fields] AND "imaging"[All Fields]) OR "autofluorescence imaging"[All Fields]) OR (("flexibilities"[All Fields] OR "flexible"[All Fields] OR "flexibles"[All Fields] OR "pliability"[MeSH Terms] OR "pliability"[All Fields] OR "flexibility"[All Fields]) AND ("spectral"[All Fields] OR "spectrally"[All Fields]) AND ("image"[All Fields] OR "image s"[All Fields] OR "imaged"[All Fields] OR "imager"[All Fields] OR "imager s"[All Fields] OR "imagers"[All Fields] OR "images"[All Fields] OR "imaging"[All Fields] OR "imaging s"[All Fields] OR "imagings"[All Fields]) AND ("colorant"[All Fields] OR "colorants"[All Fields] OR "coloration"[All Fields] OR "colorations"[All Fields] OR "colored"[All Fields] OR "coloreds"[All Fields] OR "colorful"[All Fields] OR "colorfulness"[All Fields] OR "coloring"[All Fields] OR "colorings"[All Fields] OR "colorization"[All Fields] OR "colorized"[All Fields] OR "colour"[All Fields] OR "color"[MeSH Terms] OR "color"[All Fields] OR "colourant"[All Fields] OR "colourants"[All Fields] OR "colouration"[All Fields] OR "colourations"[All Fields] OR "coloured"[All Fields] OR "coloureds"[All Fields] OR "colourful"[All Fields] OR "colourfulness"[All Fields] OR "colouring"[All Fields] OR "colourings"[All Fields] OR "colours"[All Fields] OR "colors"[All Fields]) AND ("enhance"[All Fields] OR "enhanced"[All Fields] OR "enhancement"[All Fields] OR "enhancements"[All Fields] OR "enhancer"[All Fields] OR "enhancer s"[All Fields] OR "enhancers"[All Fields] OR "enhances"[All Fields] OR "enhancing"[All Fields])) OR "iScan"[All Fields] OR (("virtual"[All Fields] OR "virtuality"[All Fields] OR "virtualization"[All Fields] OR "virtualized"[All Fields] OR "virtualizing"[All Fields] OR "virtuals"[All Fields]) AND ("chromoendoscopies"[All Fields] OR "chromoendoscopy"[All Fields])) OR ("dye-based"[All Fields] AND ("chromoendoscopies"[All Fields] OR "chromoendoscopy"[All Fields]))))) AND ((fha[Filter]) AND (fft[Filter]) AND (english[Filter] OR spanish[Filter]))

Science Direct:

((inflammatory bowel disease) OR (colitis ulcerative) OR (Crohn disease)) AND ((colitis-associated neoplasms) OR (colorectal neoplasms)) AND ((colonoscopy) OR (endoscopy)) AND ((virtual chromoendoscopy) OR (dye-based chromoendoscopy))

Scielo:

((((inflammatory bowel disease) OR (colitis ulcerative) OR (Crohn disease))) AND ((colonoscopy) OR (endoscopy))) AND ((methylene blue) OR (indigo carmine) OR (coloring agents) OR (narrow band imaging) OR (image enhancement) OR (autofluorescence imaging) OR (flexible spectral imaging color enhancement) OR (iScan) OR (virtual chromoendoscopy) OR (dye-based chromoendoscopy))

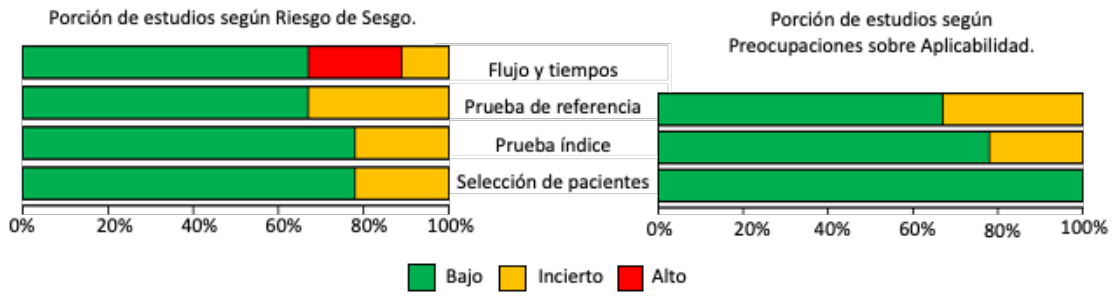
Autores	Año de publicación	Probabilidad de sesgos				Preocupación sobre la aplicabilidad de los resultados		
		Selección de los individuos	Prueba índice	Prueba de referencia	Flujo y tiempos	Selección de los pacientes	Prueba índice	Prueba de referencia
López-Serrano (25)	2021	🟡	🟢	🟢	🔴	🟢	🟢	🟢
González-Bernardo (19)	2020	🟢	🟢	🟢	🟢	🟢	🔴	🟢
Vleugels (21)	2018	🟢	🟢	🟢	🟢	🟢	🟡	🟢
Gulati(24)	2018	🟢	🟡	🟡	🟢	🟢	🟢	🟢
Iacucci (23)	2018	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Bisschops (20)	2017	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Gasia (27)	2016	🟡	🟢	🟢	🔴	🟢	🟡	🟢
Efthymiou (26)	2013	🟢	🟢	🟡	🟡	🟢	🟢	🟢
Pellisé (XX)	2011	🟢	🟡	🟡	🟢	🟢	🟢	🟡

🟢 Riesgo bajo; 🟡 riesgo incierto; 🔴 riesgo alto.

Supplementary Figure 1. Quality assessment results (QUADAS 2) of the included studies regarding likelihood of bias and concern about the applicability of results.

Figura supl. 1 picada para traducir:

Autores	Authors
Año de publicación	Year of publication
Probabilidad de sesgos	Likelihood of bias
Preocupación sobre la aplicabilidad de los resultados	Concern about the applicability of results
Selección de los individuos	Subject selection
Prueba índice	Index test
Prueba de referencia	Reference standard test
Flujo y tiempos	Flow and timing
Selección de los pacientes	Patient selection
Riesgo bajo	Low risk
Riesgo incierto	Uncertain risk
Riesgo alto	High risk



Supplementary Figure 2. Distribution of studies according to risk of bias and concern about applicability, shown as percentages of the total number of included studies.

Figura supl. 2 picada para traducir:

Porción de estudios según riesgo de sesgo	Studies according to risk of bias
Porción de estudios según Preocupaciones sobre Aplicabilidad	Studies according to applicability concerns

Flujo y tiempos	Flow and timing
Prueba de referencia	Reference standard test
Prueba índice	Index test
Selección de pacientes	Patient selection

Bajo	Low
Incierto	Uncertain
Alto	High

Supplementary Table 3.